

WHAT IS CLAIMED IS:

5 1. A method of measuring a physiological response in a cell, comprising the steps of:

- 1) introducing one or more cells in a liquid medium into a well of an electric field stimulation device, wherein said device comprising at least one transparent electrode disposed on the surface of the transparent bottom of the well;
- 10 2) labeling said cell with an optically detectable marker;
- 3) exposing said cell to repetitive electric pulses supplied by the transparent electrode and a second electrode of opposing polarity, wherein said repetitive electric pulses are of about between 250 – 1000  $\mu$ s duration at about 1 – 100 pulses/s and about 2 – 120 V amplitude, wherein said electric pulses produce a
- 15 controlled change in a physiological response of said cell;
- 4) detecting an optical signal associated with the optically detectable marker; and
- 5) comparing the optical signal measured in step (4) with an optical signal measured from a cell that is not exposed to the repetitive electric pulses.

20 2. The method of claim 1, wherein said physiological response in a cell comprises a change in the activity of an ion channel, a change in the secretion or absorption of a biological molecule by the cell, plasma membrane rearrangement, intracellular rearrangement, a change in cellular metabolism, apoptosis, or gene transcription.

3. A method of characterizing the biological activity of a candidate compound, comprising the steps of:

- 25 1) introducing one or more cells in a liquid medium into a well of an electric field stimulation device, wherein said device comprising at least one

transparent electrode disposed on the surface of the transparent bottom of the well;

- 2) labeling said cell with an optically detectable marker;
- 3) contacting the cell with a test compound;
- 5 4) exposing said cell to repetitive electric pulses supplied by the transparent electrode and a second electrode of opposing polarity, wherein said repetitive electric pulses are of about 250 to about 1000  $\mu$ s duration at about 1 to about 100 pulses/s and about 2 to about 120 V amplitude, and produce a controlled change in a physiological response of said cell;
- 10 5) detecting an optical signal associated with the optically detectable marker; and
- 6) comparing the optical signal measured from step 5) with an optical signal measured from a cell that is not contacted with the candidate compound.

4. The method of claim 3, wherein said transparent electrode comprises an electrically conductive transparent material or is a metallic optically transparent electrode.

- 15 5. The method of claim 4, wherein said electrically conductive transparent material is selected from a group consisting of indium tin oxide (ITO), zinc oxide (ZnO), SnO<sub>2</sub>, CdO, MgIn<sub>2</sub>O<sub>4</sub>, Al-doped ZnO film, a diamond thin film, and a combination thereof.

6. The method of claim 5, wherein said electrically conductive transparent material is indium tin oxide (ITO).

- 20 7. The method of claim 4, wherein said transparent electrode further comprises a layer of an insulating transparent material external to the electrically conductive transparent material.

8. The method of claim 7, wherein said insulating transparent material is a transparent dielectric, selected from silicon dioxide (SiO<sub>2</sub>), silicon nitride (Si<sub>3</sub>N<sub>4</sub>), and silicon oxynitride (SiO<sub>x</sub>N<sub>y</sub>).
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9. The method of claim 7, wherein the thickness of the insulating transparent material is about 100 Å to about 2000 Å.

10. The method of claim 3, wherein said second electrode of opposing polarity is inserted into the fluid bathing the cells inside the well, wherein a voltage applied between the transparent electrode and the second electrode creates a vertical electric field capable of stimulating cells inside the well.
- 5 11. The method of claim 10, wherein said second electrode of opposing polarity comprises an electrically conductive transparent material or is a metallic optically transparent electrode.
12. The method of claim 10, wherein said second electrode comprises an electrically conductive non-transparent material.
- 10 13. The method of claim 12, wherein said electrically conductive non-transparent material is selected from the group consisting of gold, platinum, palladium, chromium, molybdenum, iridium, tungsten, tantalum, titanium, stainless steel, carbon, graphite and polypyrrole.
14. The method of claim 3, wherein the electric field stimulation device comprises two  
15 transparent electrodes with opposite polarity that are disposed on the surface of the transparent bottom of the well, wherein a voltage applied between the two transparent electrodes creates a horizontal electric field capable of stimulating cells inside the well.
15. The method of claim 14, wherein the two transparent electrodes are fabricated to contain interdigitated fingers covering the surface of the transparent bottom of the well.
- 20 16. The method of claim 15, wherein the interdigitated fingers include a width and spacing such that a single cell can contact at least two or more electrodes of opposing polarity.
17. The method of Claim 3, wherein said physiological response is a change in the conductivity of an ion channel wherein the ion channel is selected from the group  
25 consisting of a potassium channel, a calcium channel, a chloride channel, a sodium channel, a non-specific ion channels, and a combination thereof.

18. The method of claim 17, wherein said physiological response is a change in the conductivity of a voltage-gated ion channel.
19. The method of Claim 3, wherein said optically detectable marker is a fluorescent dye, a radioactive ion, a fluorescent protein, a luminescent protein, a protein tagged with a fluorescent or luminescent epitope, or a change in the refractive index of the cells.
20. The method of Claim 3, wherein said optically detectable marker is a voltage sensor selected from the group consisting of FRET based voltage sensors, electrochromic transmembrane potential dyes, transmembrane potential redistribution dyes, radioactive ions, ion sensitive fluorescent or luminescent dyes, and ion sensitive fluorescent or luminescent proteins.
21. The method of Claim 3, wherein said cell is a eukaryotic cell.
22. The method of Claim 3, wherein said cell is a prokaryotic cell.
23. The method of Claim 3, wherein said cell is associated with a biological tissue.
24. The method of claim 3, wherein the optical signal associated with the optically detectable marker is monitored via an imaging system.
25. The method of claim 24, wherein the imaging system comprises a microscope connected to a charge-coupled device camera, a photodiode array, or a photomultiplier tube.
26. The method of claim 24, wherein the imaging system comprises a plate reader, connected to a charge-coupled device camera, a photodiode array, or a photomultiplier tube.
27. The method of Claim 3, wherein said repetitive electric pulses are supplied in a square wave-form, a sinusoidal wave-form, or a saw tooth wave-form.

28. The method of Claim 27, wherein said repetitive electric pulses are supplied in a square wave-form.
29. The method of Claim 28, wherein said repetitive electric pulses have an amplitude within the range of about 20 to about 100 V.
- 5    30. The method of Claim 28, wherein said repetitive electric pulses have a pulse duration within the range of about 250 to about 1000 per pulse.
31. The method of claim 30, wherein said repetitive electric pulses are supplied to the cell in about 750  $\mu$ s per pulse at about 8 pulses per second, and the train of pulses lasts about 3 seconds.
- 10    32. The method of claim 3, further comprising the step of coating the surface of the transparent bottom of the well with a factor to promote cell attachment.
33. The method of claim 32, wherein the factor is selected from poly-d-lysine, poly-l-lysine, collagen type 1, collagen type IV, heparin sulphate proteoglycan, laminin, fibronectin, vitronectin, gelatin or poly-l-ornithine.
- 15    34. A system for supplying electric field stimulation to a cell and optically monitoring a physiological response of the stimulated cell, comprising
- 1) an electric field stimulation device comprising a well and an transparent electrode disposed on the surface of the transparent bottom of the well;
  - 20    2) a cell labeled with an optically detectable marker placed and its bathing fluid within the well of the electric field stimulation device;
  - 3) a means for providing electrical stimulation; and
  - 4) an imaging system for detecting the optical signal from the cell.